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May 14, 2002

The Honorable Christine Todd Whitman
Administrator
U.S. Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the Epoxy Resin Systems Task Group's HPV Test Plan and Robust Summary for n-Butyl Glycidyl Ether

Dear Administrator Whitman:

The following comments on the Epoxy Resin Systems Task Group's (ERSTG's) test plan for n-butyl glycidyl ether are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than nine million Americans.

The ERSTG has sensibly grouped together the isomers n-butyl glycidyl ether and t-butyl glycidyl ether, two compounds with similar physicochemical and toxicological properties. N-butyl glycidyl ether is a skin, eye, and respiratory irritant. It has also been implicated as a mutagen in many studies.

Characterizing the health effects of glycidyl ethers has been a priority issue for the EPA for more than a decade. Since these chemicals have the highly reactive epoxides as functional groups, concern about their mutagenic properties and general toxicity has prompted much research. Given the known toxicity of n-butyl glycidyl ether, OSHA, NIOSH, and ACGIH have all set exposure limits. The OSHA TWA Permissible Exposure Limit is 50 ppm, the ACGIH Threshold Limit Value is 25 ppm, and the NIOSH recommends a 15-minute exposure limit of 5.6 ppm. Although information on the developmental toxicity of n-butyl glycidyl ether is available, the ERSTG has proposed to conduct a developmental toxicity test, which would kill 960 animals.

The following terms of the October 1999 Agreement are violated by the ERSTG test plan:

1. In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.
2. Participants shall maximize the use of existing and scientifically adequate data to minimize

further testing.

The ERSTG's proposal to test n-butyl glycidyl ether is inappropriate, because information is available to address the reproductive and developmental toxicity endpoints. A dominant lethal assay cited in the ERSTG's test plan found no significant dose-related changes either in pregnancy rates or in average number of implants per pregnant female. However, there was evidence of an increase in fetal death rates by the end of the first week after the highest dosage was administered.¹

In a modified dominant lethal and pathology study of mice, significant differences were observed between mice dosed with n-butyl glycidyl ether and control animals for the following effects: pregnancy rates, average implants per pregnant female, proportion of dead implants. No significant differences were observed between treated and control animals in the following: pregnancy rates; gross pathology of males; histopathology of the liver, lung, and testes; and numbers of dead cells and necrotic tubules.²

To glean the most information from the available data, the ERSTG should consider evaluating the toxicity of the butyl ether compounds in the context of its alkyl glycidyl ether category. While the alkyl glycidyl ethers are larger substances and have different physical chemical properties, these chemicals exhibit similar mechanisms of toxicity, with the epoxide being the relevant toxic moiety. An assessment of the associations of structure, physicochemical properties, and toxicity would maximize existing data and could obviate the requirement of future tests.

The HPV program is a screening level hazard identification program. Many studies have already been conducted that evaluate various potential adverse effects of this toxic chemical. N-butyl glycidyl ether is a respiratory, dermal, and ocular irritant. Studies have shown that the chemical is associated with genotoxic effects, reproductive toxicity, and developmental toxicity. Occupational safety and health exposure limits have been established based on the available information. Additional tests would not expand our knowledge of the toxicological profile of this chemical in a meaningful way.

Thank you for your attention to these comments. I can be reached at 202-686-2210, ext. 302, or via e-mail at ncardello@pcrm.org. Correspondence may be sent to my attention to PCRM, 5100 Wisconsin Ave., N.W., Suite 400, Washington, DC 20016.

Sincerely,

Nicole Cardello, M.H.S.
Staff Scientist

References

1. Whorton EB Jr, Pullin TG, Frost AF, Onofre A, Legator MS, Folse DS. Dominant lethal effects of n-butyl glycidyl ether in mice. *Mutat Res* 1983;124(3-4):225-33.
2. University of Texas. Modified Dominant Lethal Assay and Pathology Study of Mice Exposed to n-Butyl Glycidyl Ether. EPA Document No. 878210058, Fiche No. OTS0206194. 1979.